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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/569,847	04/10/2006	Jae Yong Han	50413/013001	2565

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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
05/12/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/569,847	HAN ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *16-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 11, 2009 that includes a response to the Office action dated June 11, 2008, has been entered. Claim 1 has been amended, and claims 20-25 newly added. No claims were cancelled. Accordingly, claims 1-25 are pending in the Application. Claims 16-19 stand withdrawn from further consideration without traverse, as being drawn to non-elected subject matter.

Claims 1-15 and 20-25 are under current examination. The claims have been examined commensurate with the elected species of "gonadal stromal cell", "stem cell factor", "chicken" and "staining with α6-integrin antibody".

Withdrawn Claim Rejections - 35 USC § 102

Claims 1, 2, 4-10, 12, 13 and 14 were rejected under 35 U.S.C. 102(e) as being anticipated by Baguisi et al. (U.S. Patent Publication No.: 2002/0162134 effective filing date: Feb. 16, 2001), in the previous office actions dated August 30, 2007 and June 11, 2008. Applicants have amended base claim 1 to limit the avian testis to age up to 70 weeks, that is not expressly taught by Baguisi et al. Thus, the rejection is hereby withdrawn. The claims are however subject to a new rejection over the prior art, as set forth below.

Withdrawn Claim Rejections - 35 USC § 103

Claims 1, 3, 11 and 15 were rejected under 35 U.S.C. §103(a) as being unpatentable over Baguisi et al. (U.S. Patent Publication No.: 2002/0162134 effective filing date: Feb. 16, 2001), in

view of Shinohara et al. (U.S. Patent Publication No: 2006/0265774; effective filing date April 15, 2003), in the previous office actions dated August 30, 2007 and June 11, 2008. Applicants have amended base claim 1 to limit the avian testis to age up to 70 weeks, that is not expressly taught by the cited references. Thus, the rejection is hereby withdrawn. The claims are however subject to a new rejection over the prior art, as set forth below.

New Claim Rejections - 35 USC § 103

Claims 1, 2, 4-10, 12-15 and 20-25 are newly rejected under 35 U.S.C. §103(a) as being unpatentable over Baguisi et al. (U.S. Patent Publication No.: 2002/0162134 effective filing date: Feb. 16, 2001), in view of Shinohara et al. (PNAS 97:8346-8351; 2000; henceforth Shinohara 2000).

The claims encompass a method for isolation and culture of chicken spermatogonial stem cells (SSCs) from adult testis.

Baguisi et al. describe isolated avian gonadal cells from the testes (Title and Abstract), and methods of isolating and culturing the same. Specifically teaching the harvest of the gonads from chick embryos and their grouping by sex (corresponding to preparation of chicken testis), and their dispersion by standard trypsinization procedure and culture in tissue culture plates (paragraph [0035], p. 4; limitation of claims 1(b), 1(c) and 2). Further teaching: "The PGCs can either be co-cultured with gonadal stromal cells (limitation of claims 4-6) or separated prior to culture on plates at 37° C." (limitation of claim 12). "The PGCs were cultured in DMEM with high glucose content and supplemented with 10% FBS, 5% chicken serum and growth factors (basic Fibroblast Growth Factor, Insulin Growth Factor-1 and Stem Cell Factor at 10 ng/ml and murine Leukemia Inhibitory Factor at 10units /ml to maintain their germ cell state." (paragraph [0050], p. 6; limitation of claims 7-10). The terms insulin growth factor 1 and insulin-like growth factor 1 appear interchangeably in the prior art. Baguisi et al. state that chicken PGCs have a high glycogen content and thus are identifiable by periodic acid Schiff staining (paragraph [0050], pp. 5-6; limitation of claim 14).

While Baguisi et al. do not describe deriving the stem cells from an adult aged up to 70 weeks, the isolation of spermatogonial stem cells from adult testis was known in the prior art.

Shinohara 2000 describes the enrichment and selection of spermatogonial stem cells from adult cryptorchid testis (Abstract) and adult wild type testis (Fig.1, p. 8347 and second column, p. 8348). Shinohara 2000 further state that spermatogonial stem cells arise from PGCs, and both express α6-integrin, that make possible their enrichment and isolation (second column, p. 8350). As the prior art of record teaches that spermatogonial stem cells are present in both the embryo and adult stages of animals, it is not considered inventive to isolate said cells from any particular stage of development, form 2 weeks, up to 70 weeks. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In the instant case, the non-criticality of the stage of isolation is evidenced by the broad range of 2 to 70 weeks claimed. Moreover, the instant specification states: "Testicular cells of aves such as chicken show similar culture pattern to those of mammals" (pp. 32-33, bridging); and that it has been reported that spermatogonial stem cells of mice and calf were cultured for about 5 months (p. 33, lines 21-24).

Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine the teachings of Baguisi et al. and Shinohara 2000 (as both describe methods for the isolation of sperm stem cells), and to culture the isolated spermatogonial stem cells for an extended period, with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would be motivated to isolate sperm stem cells from an adult testis, because such is specifically taught by Shinohara 2000, and would result in a greater enrichment of spermatogonial stem cells, versus PGCs.

Claims 1, 3 and 11 are newly rejected under 35 U.S.C. §103(a) as being unpatentable over Baguisi et al. (U.S. Patent Publication No.: 2002/0162134 effective filing date: Feb. 16, 2001), in view of Shinohara et al. (PNAS 97:8346-8351; 2000; henceforth Shinohara 2000), as applied to claims 1, 2, 4-10, 12-15 and 20-25 above, and further in view of Shinohara et al. (U.S. Patent Publication No: 2006/0265774; effective filing date April 15, 2003; henceforth Shinohara '774).

Baguisi et al. describe isolated avian gonadal cells from the testes (Title and Abstract), and methods of isolating and culturing the same. Shinohara 2000 describes the enrichment and selection of spermatogonial stem cells from adult cryptorchid testis (Abstract) and adult wild type testis (Fig.1, p. 8347 and second column, p. 8348). While Baguisi et al. additionally describe the harvest of chick gonads and their dispersion by standard trypsinization procedure and culture in tissue culture plates (paragraph [0035], p. 4), they do not describe treating the tissue with a mixture of collagenase and trypsin and the inclusion of an antioxidant in the culture medium.

Shinohara '774 describe a method for growing spermatogonial stem cells *in vitro* (Abstract), wherein the testis is totally digested with collagenase, trypsin and DNase (paragraph [0065], p. 6; limitation of claim 3), and the dissociated cells are cultured in medium containing fetal calf serum and 2-mercaptoethanol (an antioxidant; paragraph [0102], p. 9; limitation of claim 11). To confirm the properties of the cells cultured, flow cytometry was carried out using antibodies to various markers that included rat antihuman α6-integrin (paragraph [0104], p. 9).

Thus, Shinohara '774 cures the deficiency in Baguisi et al. for tissue preparation using collagenase and trypsin, and culturing the stem cells in the presence of an antioxidant.

Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine the teachings of Baguisi et al., Shinohara 2000 and Shinohara '774 (as all describe methods for the isolation sperm stem cells), with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would be motivated to isolate sperm stem cells from an avian testis using a combination of collagenase and trypsin, because said combination would be more efficient than using trypsin alone. A person of skill in the art would be further motivated to culture sperm stem cells in the presence of 2-ME, because the inclusion of an antioxidant in the medium was known to stabilize the cultured cells.

Response to Arguments

To the extent that Applicants' arguments may apply to the new rejections set forth above, they are addressed as follows:

Applicants traverse the rejection, arguing that there is no substantial description as to specific procedures to actually isolate or prepare sperm stem cells from the testes of adult chicken in the Baguisi reference, and the entire context of Baguisi makes it clear that embryonic cells alone, and not adult cells. Applicants' arguments have been fully considered, but are not found persuasive.

In response, it should be noted that the deficiency in Baguisi et al. for adult testis as the source of the spermatogonial stem cells is cured by the reference of Shinohara 2000, disclosed above.

With regard to the combination of references of Baguisi et al. (teaching chicken PGCs), and Shinohara '774 (teaching mouse spermatogonial stem cells), Applicants refer to MPEP 2143.01, and argue that the mere fact that references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. Such is not found persuasive, because the prior art had established that spermatogonial stem cells arise from PGCs, and that the adult testis contains stem cells at various stages of differentiation. It should additionally be noted that the instant claims are not limited to adult avian testis, as they include claims to 2-week old chicken, that cannot be considered an adult.

Applicants argue that Baguisi et al.'s statement that these techniques are still in their early developmental stage and may be difficult to adapt to the uniquely different reproductive systems of birds, supports the unpredictability of the present invention. Such is not found persuasive, because the paragraph cited by Applicants relates to the production of cloned animals by nuclear transfer in mammal, and is not commensurate with a method of isolating and culturing spermatogonial stem cells. Further, for an obviousness rejection, only a reasonable expectation of success is considered sufficient.

Applicants argue that in paragraph [0006], Shinohara '774 state that in any animal other than mice (for example, domestic animals such as swine and bovines and primates), no ES cells capable of producing germ cells have been collected to date, nor is there any report of knockout achieved by this technique. In response, it is noted that such is irrelevant to the instantly claimed method, that does not require ES cells or production of knockouts using ES cells.

Applicants argue that in paragraph [0007], Shinohara '774 state "For animals other than mice, however, the success rate (of gene injection) is very low (for example, around 1% for swine and 1% or less for bovines) and the method is very expensive and unrealistic." In response, it should be noted that the paragraph is referring to the production of transgenics, not required for the instant method of isolating and culturing stem cells.

Applicants argue that in paragraph [0010] of Shinohara '774, there is no description as to any other animal stem cell than mouse or rat. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The teachings of Baguisi et al. regarding the isolation of chicken testes cells thus cannot be dismissed. It should additionally be noted that the instant specification states: "Testicular cells of aves such as chicken show similar culture pattern to those of mammals" (pp. 32-33, bridging); and that it has been reported that spermatogonial stem cells of mice and calf were cultured for about 5 months (p. 33, lines 21-24).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicants argue that the Declaration of Jae Yong Han explains the long but unresolved need for long-term culture of SSCs from the avian testes. However, such is not found persuasive because paragraphs [0110] and [0111] of Baguisi et al. describing culture of chicken germ cells for over 3 months in repeated subcultures. Further, the isolation of SSCs is described in the newly applied prior art of Shinohara 2000. Additionally, the physiological differences between birds and mice are not relevant here, because the only issue regarding the teachings of Baguisi et al. is the stage of isolation of germ cells from the testes. And such deficiency is addressed by the teachings of Shinohara 2000.

Conclusion

Claims 1-15 and 20-25 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Examiner, Art Unit 1633